Dkt. 00052CIP

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of :
PATRICK MAHY et al
Serial No. : **09/536,153** Group Art Unit : 1644
Filed : **March 28, 2000** Examiner : G. Ewoldt

For : **ANTIGEN VECTORS IN THE FORM OF MULTILAMELLAR VESICLES AND COMPOSITIONS CONTAINING ANTIGENS ENCAPSULATED IN THESE VESICLES**

DECLARATION UNDER 37 CFR 1.132

Honorable Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Anne Bernheim-Groswasser, declare as follows:

I am a citizen of Israel residing in France at Institut Curie, Physico-Chimie Curie UMR 168, 11 rue Pierre et Marie Curie, 75231 PARIS.

I am a researcher (from the 1st October 2002) at the Chemical Engineering Dept. at Ben-Gurion University - Beer-Sheva 84105, Israel and I am now at Curie Institute in Paris as a post-doctoral fellow, where I am carrying out research in the field of condensed matter physics and biophysics.

I have a scientific expertise in microscopy techniques including light microscopy (fluorescence, phase contrast, DIC and Cryo-TEM).

I have examined micrographs which were submitted to me by the Applicants of the present application and copies of which are attached hereto as Figures 1, 2 and 3:

- FIGURE 1 is a freeze fracture electron micrograph representing the structure of classical multilamellar vesicles MLV (corresponding to figure 3A of US 4,975,282 assigned to the Liposome Company, Inc);
- FIGURE 2 is a freeze fracture electron micrograph of the vesicles of the present invention in condensed phase (before their dispersion in a solvent); and
- FIGURE 3 is a photograph of an Applicants' vesicle under cryo-TEM, the vesicle being a phospholipidic vesicle incorporating a protein, namely HSA protein, which was used in example 1 of the present application.

Comparison of Figures 1 and 2 attached clearly shows the structural differences between the two types of vesicles:

In the classical MLVs, a relatively large core of water (or solution) is enclosed (this is clearly seen in Figure 1). Moreover, the lipidic membrane is folded up, and this can occur only if the bilayers are not regularly stacked. Consequently, the bilayers shown in Figure 1 cannot be considered as concentric and regularly stacked from the center to the periphery.

In the vesicle of the present invention, the bilayers are concentric and extend from the very center of the vesicle to its periphery, which is not the case of classical MLVs.

Figure 3 is a cryo-TEM photograph which enables visualization the structure of an individual vesicle according to the present application; Figure 2 is a freeze fracture electron microscopy photograph, showing the structure of the vesicles before their dispersion. Figure 3 shows that even after their

dispersion in a solvent medium, the vesicles maintain their uniform structure.

In view of these considerations, the structure of the two types of vesicles is clearly different and the distinguishing features of the Applicants' vesicles are:

1. The uniformity of the structure and
2. The absence of real aqueous core since the stacking of bilayers clearly extend from the center to the periphery of the vesicle.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Anne Bernheim-Groswasser

Anne Bernheim-Groswasser

dated: 3/7/02

FIGURE 1

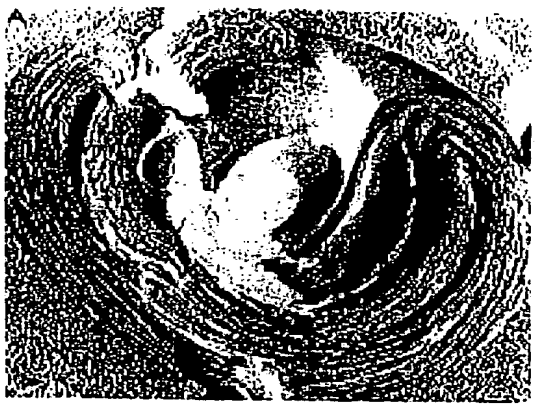

FIGURE 2

FIGURE 3